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## OPIATE RECEPTOR SUBTYPES



| guines-pig Keum                            |  | phancyclidine  | N-allyinormetazocine<br>(SKF 10,047) |                                    |  |                           | ιĝ                  |
|--|--|--|--------------------------------------|------------------------------------|--|---------------------------|---------------------|
| rat vas deferens<br>guines-pig Beum        | næloxone                                       | Bendorphin   | β-endorphin                          | pro-opiometanocortin<br>(POMC)     | as above   | p-endorphin               |                     |
| rabbit<br>vas deferens<br>guinaa-pig ileum | naloxons<br>WIN-44,441-3<br>MR-2266            | U 50,488<br>dynorphin <sub>t=1</sub> ,               | ketocyclazocine**                    | prodynorphin<br>(proenkephalin B)  | Tyr-Gly-Gly-Phe-Leu-Arg-Arg-Be-Arg-Pro-Lys-Leu<br>Lys-Trp-Asp-Asn-Gln  | dynorphin <sub>1-17</sub> | ×                   |
| guines-pig lieum                           | 100/8/11 mu                                    |  |                                      |                                    | The Old Carps of A Carps   |                           | 1                   |
| mouse<br>via deferent                      | nalozone<br>ICI 154,129<br>ICI 174 aca         | P.Ale <sup>®</sup> D. Beufunkaphalin<br>(DADL)       | [Leu]enkephalin                      | proenkephalin A                    | Tyr-Gly-Gly-Phe-Leu  | l- ujenkephalin           | 0                   |
|  |  |  |                                      | proentephalin A                    | Tyr-Giy-Giy-Phe-Met  | [Met]enkephalin           |                     |
| grinea-pig<br>Heum                         | natox onazina<br>6-funato examina<br>natoxona* | memphicaptin<br>Tyro-Azidiy-WMe-Phe<br>Glycal (DAGO) | morphine                             | pro-opiomalanocortin<br>(POMC)     | Tyr-Gly-Gly-Bhet-Thr-Ser-Glu-Lys-Ser-Gla-Thr-<br>Pro-Leu-Val-Thr-Leu-Phe-Lys-Asn<br>Ala-lie-Re-Lys-Asn-Ala-His-Lys-Lys-Gly-Gla | β-endorphin               | T                   |
| In-vitro assay<br>system                   | Selective<br>antagonists                       | Selective<br>agonists                                | Prototype<br>agonist                 | Endogenous<br>agonist<br>precursor | Endogenous agonist structure   | Endogenous                | Receptor<br>subtype |
|  |  |  |                                      |                                    |  |                           |                     |

f Signa receptors may not be exclusively opioid. • decreasing order of potency of naturone approximately 115 48 for u.∴.\ (e potency is betreesen u and \). ••Authough ketocyclaz-ocine is the prototype benzomorphan agonist, it has been proposed that benzomorphan a egonist may bind @Renewdy than other putative a egonists. IG 154328 - AMERINATIO GOVERNO FOR CONTRACTOR AND ADPORTED ON THE ACTUAL SENSON OF THE CONTRACTOR OF PROPERTY SETTEMBLY SETTEM

behavioural

## association with receptor subtypes Effects of opiates:

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This chart represents an attempt to integrate three schools of thought regarding the biological identities and fu..ctions of multiple opiate receptor subtypes. The accuracy of these estimates of functional specifier is only as precise as the ligands employed and may vary according to experimental conditions. At high dose, most of the ligands indicated in the table above cross-react with other receptor subtypes.

receptives provide a dominon binding site for alkaloid and peptide opiates, whereas selectively different effects of opiate ligands may be mediated by separate, low affinity sites (e.g. b, h), if and i). Pert and tes and interconvert between wand\conformations. Type II receptors are fixed in a 6 conformation pattern. It is possible that Type I receptors colleagues have further identified Type I receptors (high affinity, adenytate cyclase coupled) which may demonstrate fluctuating affini-

Gundan St. J. R. S.

It has recently been indicated that it and it binding sites may be allosterically coupled or interconvert. Holaday and colleagues have extended the observations to demonstrate functional interactions. are similar to gr receptors as Insted among it, it and 5 binding sites

- Direct magnement shown - Poss ble on a serveni The effect of opiates on the immune response is an eminvestigation and designation of receptor subtypes in responses is very speculative.

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